

### **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

1. (Withdrawn) A composition comprising a narcotic analgesic and a nontoxic VR1 antagonist.
2. (Withdrawn) The composition of claim 1 wherein the narcotic analgesic is selected from alfentanyl, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, meperidine, metazocine, methadone, metopon, morphine, opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan, thebaine, their mixtures and their pharmaceutically acceptable salts and hydrates.
3. (Withdrawn) The composition of claim 1, wherein the narcotic analgesic is selected from codeine, fentanyl, hydrocodone, meperidine, morphine, oxycodone, their mixtures and their pharmaceutically acceptable salts and hydrates.
4. (Withdrawn) The composition of claim 1, wherein the VR1 antagonist is not a vanilloid compound.
5. (Withdrawn) The composition of claim 1, wherein the VR1 antagonist exhibits a  $K_i$  value of 1 micromolar or less in a capsaicin receptor binding assay.
6. (Withdrawn) The composition of claim 1, wherein the VR1 antagonist exhibits a  $K_i$  value of 100 nanomolar or less in a capsaicin receptor binding assay.
7. – 11. (Cancelled)
12. (Withdrawn) A packaged pharmaceutical composition, comprising:
  - (i) a container holding a composition comprising a nontoxic VR1 antagonist; and
  - (ii) instructions indicating that the VR1 antagonist is to be administered to a patient contemporaneously with administration of an addictive substance.

13. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the addictive substance is a narcotic analgesic.

14. (Withdrawn) The packaged pharmaceutical composition of claim 12, further comprising a narcotic analgesic.

15. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the composition is formulated for oral administration.

16. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the VR1 antagonist is not a vanilloid compound.

17. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the VR1 antagonist exhibits a  $K_i$  of 1 micromolar or less in a capsaicin receptor binding assay.

18. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the VR1 antagonist exhibits a  $K_i$  of 100 nanomolar or less in a capsaicin receptor binding assay.

19. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the instructions indicate that the VR1 antagonist is to be used for inhibiting the development of tolerance to an addictive substance in a patient.

20. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the instructions indicate that the VR1 antagonist is to be used for inhibiting the development of dependence on an addictive substance in a patient.

21. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the instructions indicate that the VR1 antagonist is to be used for enhancing pain relief upon administration of addictive substance to a patient.

22. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the VR1 antagonist is present in a tolerance-reducing amount.

23. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the VR1 antagonist is present in a dependence-reducing amount.

24. (Withdrawn) The packaged pharmaceutical composition of claim 12, wherein the VR1 antagonist is present in a pain relief-enhancing amount.

25. (Withdrawn) A packaged pharmaceutical composition, comprising:  
(i) a nontoxic VR1 antagonist;  
(ii) a narcotic analgesic; and  
(iii) instructions indicating that the VR1 antagonist and narcotic analgesic are to be administered to a patient for the treatment of pain.

26. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist and narcotic analgesic are present in the same composition.

27. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist and narcotic analgesic are present in different containers.

28. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist and narcotic analgesic are formulated for oral administration.

29. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist is not a vanilloid compound.

30. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist exhibits a  $K_i$  of 1 micromolar or less in a capsaicin receptor binding assay.

31. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist exhibits a  $K_i$  of 100 nanomolar or less in a capsaicin receptor binding assay.

32. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist is present in a tolerance-reducing amount.

33. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist is present in a dependence-reducing amount.

34. (Withdrawn) The packaged pharmaceutical composition of claim 25, wherein the VR1 antagonist is present in a pain relief-enhancing amount.

35. (Withdrawn) The composition of claim 26 wherein the narcotic analgesic is selected from alfentanil, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, meperidine, metazocine, methadone, metopon, morphine, opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan, thebaine, their mixtures and their pharmaceutically acceptable salts and hydrates.

36. (Withdrawn) The packaged pharmaceutical composition of claim 35, wherein the narcotic analgesic is selected from codeine, fentanyl, hydrocodone, meperidine, morphine, oxycodone, their mixtures and their pharmaceutically acceptable salts and hydrates.

37. (Withdrawn) The packaged pharmaceutical composition of claim 25 in sustained release dosage form.

38. (Withdrawn) A method of treating pain in a patient, comprising administering to a patient, simultaneously or sequentially in either order;

(i) a narcotic analgesic; and

(ii) a nontoxic VR1 antagonist;

and thereby providing pain relief to the patient.

39. (Withdrawn) The method of claim 38, wherein the narcotic analgesic is selected from alfentanil, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, metazocine, methadone, metopon, meperidine, morphine, opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan, thebaine, their mixtures and their pharmaceutically acceptable salts and hydrates.

40. (Withdrawn) The method of claim 38, wherein the VR1 antagonist is not a vanilloid compound.

41. (Withdrawn) The method of claim 38, wherein the VR1 antagonist exhibits a  $K_i$  value of 1 micromolar or less in a capsaicin receptor binding assay

42. (Withdrawn) The method of claim 38, wherein the VR1 antagonist exhibits a  $K_i$  value of 100 nanomolar or less in a capsaicin receptor binding assay.

43. (Original) A method for inhibiting the development of tolerance to a narcotic analgesic in a patient, comprising administering to a patient, simultaneously or sequentially in either order;

(i) a narcotic analgesic; and

(ii) a tolerance-reducing amount of a nontoxic VR1 antagonist;

and thereby inhibiting the development of tolerance to the narcotic analgesic.

44. (Original) The method of claim 43, wherein the narcotic analgesic is selected from alfentanil, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, meperidine, metazocine, methadone, metopon, morphine, opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan, thebaine, their mixtures and their pharmaceutically acceptable salts and hydrates.

45. (Original) The method of claim 43, wherein the VR1 antagonist is not a vanilloid compound.

46. (Currently amended) The method of claim 43, wherein the VR1 antagonist exhibits a  $K_i$  value of 1 micromolar or less in a capsaicin receptor binding assay.

47. (Original) The method of claim 43, wherein the VR1 antagonist exhibits a  $K_i$  value of 100 nanomolar or less in a capsaicin receptor binding assay.

48. (Original) A method for inhibiting the development of dependence on a narcotic analgesic in a patient, comprising administering to a patient, simultaneously or sequentially in either order;

(i) a narcotic analgesic; and

(ii) a dependence-reducing amount of a nontoxic VR1 antagonist;

and thereby inhibiting the development of dependence on the narcotic analgesic.

49. (Original) The method of claim 48, wherein the narcotic analgesic is selected from alfentanil, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, meperidine, metazocine, methadone, metopon, morphine, opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan, thebaine, their mixtures and their pharmaceutically acceptable salts and hydrates.

50. (Original) The method of claim 48, wherein the VR1 antagonist is not a vanilloid compound.

51. (Original) The method of claim 48, wherein the VR1 antagonist exhibits a  $K_i$  value of 1 micromolar or less in a capsaicin receptor binding assay.

52. (Original) The method of claim 48, wherein the VR1 antagonist exhibits a  $K_i$  value of 100 nanomolar or less in a capsaicin receptor binding assay.

53. (Withdrawn) A method for enhancing narcotic analgesic-induced pain relief in a patient, comprising administering to a patient, simultaneously or sequentially in either order;

(i) a narcotic analgesic; and

(ii) a pain-relief enhancing amount of a nontoxic VR1 antagonist;

and thereby enhancing narcotic analgesic-induced pain relief in the patient.

54. (Withdrawn) The method of claim 53, wherein the narcotic analgesic is selected from alfentanil, alphaprodine, anileridine, bezitramide, codeine, dihydrocodeine, diphenoxylate, ethylmorphine, fentanyl, heroin, hydrocodone, hydromorphone, isomethadone, levomethorphan, levorphanol, meperidine, metazocine, methadone, metopon, morphine, opium, oxycodone, oxymorphone, pethidine, phenazocine, piminodine, racemethorphan, racemorphan, thebaine, their mixtures and their pharmaceutically acceptable salts and hydrates.

55. (Withdrawn) The method of claim 53, wherein the VR1 antagonist is not a vanilloid compound.

56. (Withdrawn) The method of claim 53, wherein the VR1 antagonist exhibits a  $K_i$  value of 1 micromolar or less in a capsaicin receptor binding assay.

57. (Withdrawn) The method of claim 53, wherein the VR1 antagonist exhibits a  $K_i$  value of 100 nanomolar or less in a capsaicin receptor binding assay.

58. (Withdrawn) A method for treating withdrawal symptoms resulting from prior administration of an addictive substance in a patient, comprising administering a nontoxic VR1 antagonist to a patient experiencing or susceptible to withdrawal symptoms, and thereby decreasing severity of the withdrawal symptoms in the patient.

59. (Withdrawn) A single dose pharmaceutical composition for the treatment of a patient experiencing pain comprising a combination of a VR1 antagonist and at least one analgesic selected from the group consisting of less than about 25 mg of anileridine, less than about 25 mg of codeine, less than about 40 mg of dextropropoxyphene, less than about 25 mg of dihydrocodeine, less than about 4 mg of diphenoxylate, less than about 20 $\mu$ g of fentanyl, less than about 2 mg of hydrocodone, less than about 1.5 mg of hydromorphone, less than about 0.8 mg of levorphanol, less than about 20 mg of meperidine, less than about 4 mg of methadone, less than about 7.5 mg of morphine, less than about 2 mg of oxycodone, less than about 0.8 mg of oxymorphone, less than about 0.8 mg of oxymorphone, less than about 40 mg of pethidine.

60. (New) The method of claim 43, wherein the VR1 antagonist is non-peptide.

61. (New) The method of claim 48, wherein the VR1 antagonist is non-peptide.

62. (New) The method of claim 43, wherein the VR1 antagonist is multi-aryl.

63. (New) The method of claim 48, wherein the VR1 antagonist is multi-aryl.